

What is claimed is:

T06040-04062360

Claims

1. A method for decreasing cell death or toxicity, said method comprising the step of contacting a cell or an animal expressing an expanded polyglutamine repeat with diphenyldiazo-bis-alpha-naphthylaminesulfonate, or a pharmaceutically effective derivative or salt thereof, in an amount sufficient to decrease said cell death or toxicity.

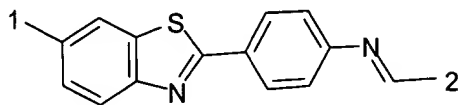
2. A method for decreasing aggregates or inclusions formed by expanded polyglutamine repeats in a cell or animal, said method comprising the step of contacting a cell or animal expressing an expanded polyglutamine repeat with diphenyldiazo-bis-alpha-naphthylaminesulfonate, or a pharmaceutically effective derivative or salt thereof, in an amount sufficient to decrease said aggregates or inclusions.

3. The method of claim 1 or 2, wherein said expanded polyglutamine repeat is resistant to at least one of the compounds chosen from the group consisting of minocycline, daunomycin, rolitetracycline, Chrysamine G, iota-carrageenan, and dextran.

4. A method for decreasing cell death or toxicity, said method comprising the step of contacting a cell or an animal expressing an amyloidogenic protein with any of bromocriptine mesylate; haloperidol; nabumetone; primidone; hydrocortisone; phenazopyridine; R-(-)-deprenyl hydrochloride; 6a-methylprednisolone 21-hemisuccinate; digoxin; azathioprine; D-cycloserine; red clover; magnesium oxide; N-vanillylnonanamide; neostigmine methyl ether; a

pharmaceutically effective derivative, salt, or isomer thereof; or a compound having the formula selected from any of:

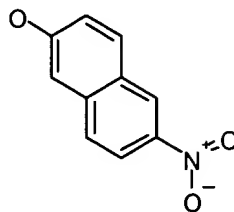
5



(1)

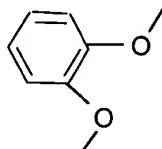
10

wherein 1 is CH₃ or H, and 2 is

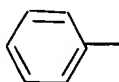


or wherein 1 is CH₃, and 2 is

15

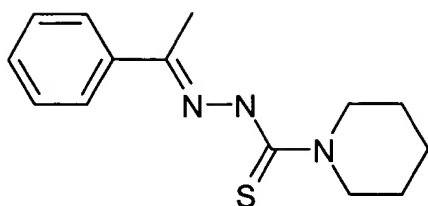


or wherein 1 is CH₃, and 2 is



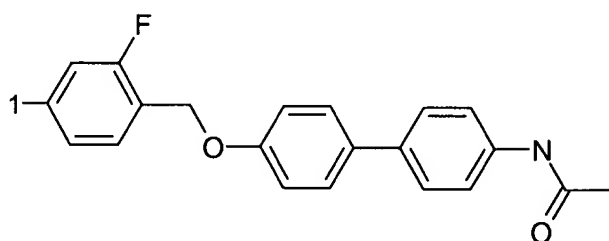
20

or a pharmaceutically effective derivative, salt, or isomer thereof;



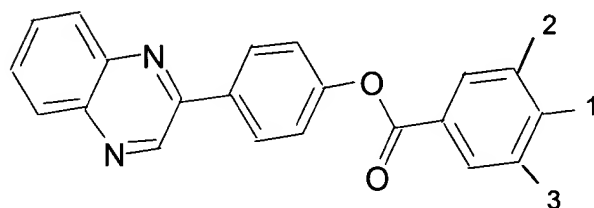
(2)

or a pharmaceutically effective derivative, salt, or isomer thereof;



(3)

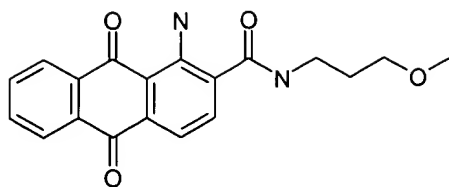
wherein 1 is H or NO₂, or a pharmaceutically effective derivative, salt, or isomer thereof;



(4)

wherein 1 is Cl, and 2 and 3 are H; or wherein 1 and 3 are H, and 2 is NO₂; or

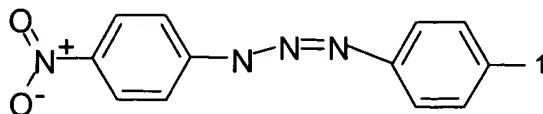
wherein 1 is Br, 2 is H, and 3 is NO₂; or wherein 1 is Cl, 2 is H, and 3 is Br, or a pharmaceutically effective derivative, salt, or isomer thereof;



(5)

5

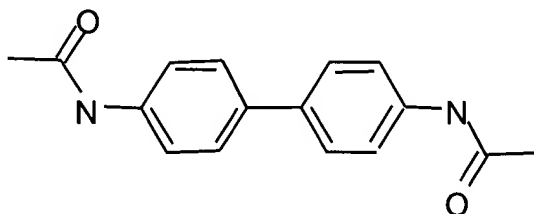
or a pharmaceutically effective derivative, salt, or isomer thereof;



(6)

10

wherein 1 is NO₂, Br, or O₂, or a pharmaceutically effective derivative, salt, or isomer thereof;

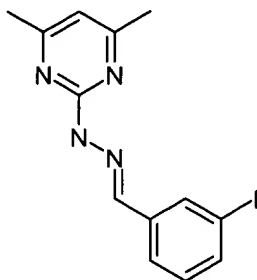


(7)

15

20

or a pharmaceutically effective derivative, salt, or isomer thereof

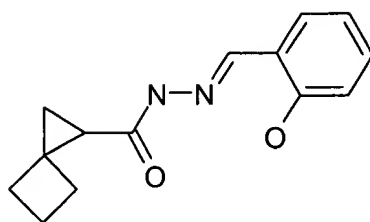


(8)

25

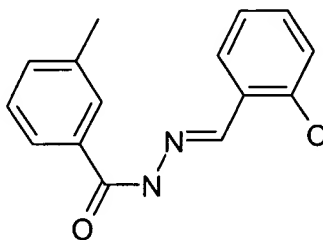
or a pharmaceutically effective derivative, salt, or isomer thereof;

5



9

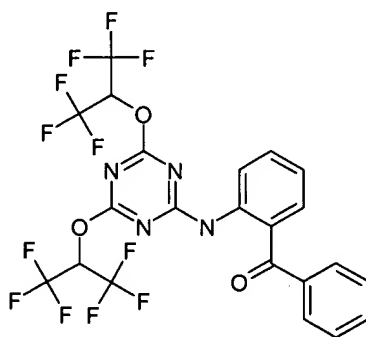
10 or a pharmaceutically effective derivative, salt, or isomer thereof;



10

15

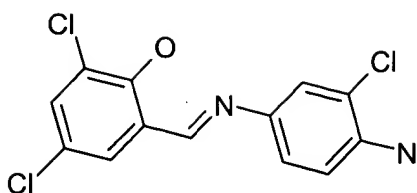
or a pharmaceutically effective derivative, salt, or isomer thereof;



11

20

25 or a pharmaceutically effective derivative, salt, or isomer thereof; or



(11)

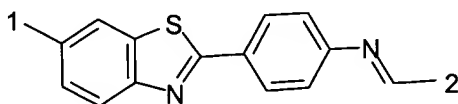
5

or a pharmaceutically effective derivative, salt, or isomer thereof, in an amount sufficient to decrease said cell death or toxicity, and wherein if said compound is haloperidol, phenazopyridine, or R-(-)-deprenyl, then said amyloidogenic protein is not beta-amyloid.

10

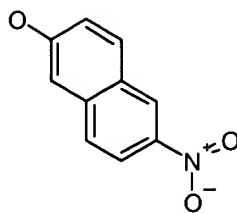
5. A method for decreasing aggregates or inclusions formed by an amyloidogenic protein in a cell or animal, said method comprising the step of contacting a cell or an animal expressing an amyloidogenic protein with any of bromocriptine mesylate; haloperidol; nabumetone; primidone; hydrocortisone; phenazopyridine; R-(-)-deprenyl hydrochloride; 6a-methylprednisolone 21-hemisuccinate; digoxin; azathioprine; D-cycloserine; red clover; magnesium oxide; N-vanillylnonanamide; neostigmine methyl ether; a pharmaceutically effective derivative, salt, or isomer thereof; or a compound having the formula selected from any of:

20

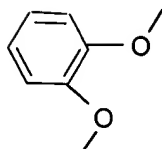


25

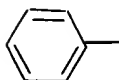
wherein 1 is CH₃ or H, and 2 is



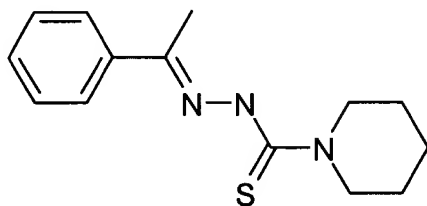
5 or wherein 1 is CH₃, and 2 is



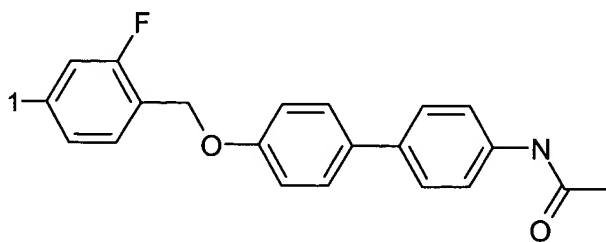
or wherein 1 is CH₃, and 2 is



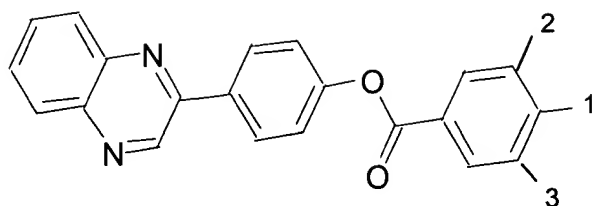
or a pharmaceutically effective derivative, salt, or isomer thereof;



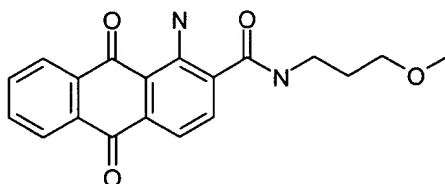
15 or a pharmaceutically effective derivative, salt, or isomer thereof;



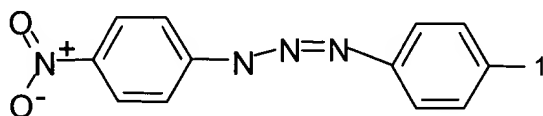
wherein 1 is H or NO₂⁻, or a pharmaceutically effective derivative, salt, or isomer thereof;



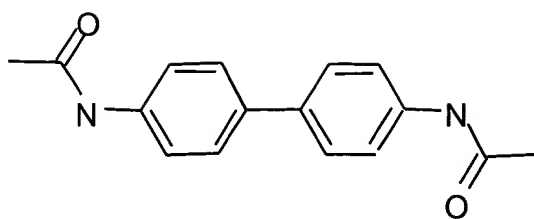
wherein 1 is Cl, and 2 and 3 are H; or wherein 1 and 3 are H, and 2 is NO₂; or
 wherein 1 is Br, 2 is H, and 3 is NO₂; or wherein 1 is Cl, 2 is H, and 3 is Br, or a
 pharmaceutically effective derivative, salt, or isomer thereof;



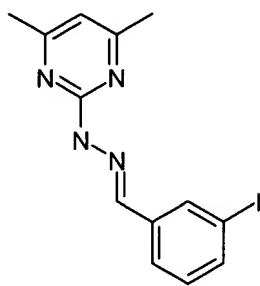
or a pharmaceutically effective derivative, salt, or isomer thereof;



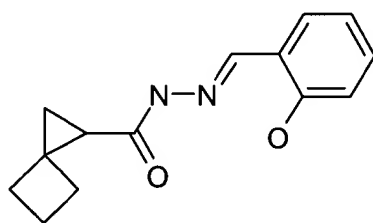
wherein 1 is NO₂, Br, or O₂, or a pharmaceutically effective derivative, salt, or
 isomer thereof;



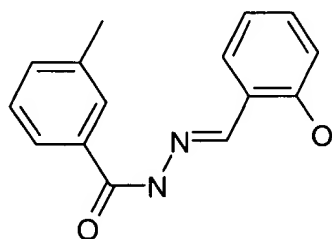
or a pharmaceutically effective derivative, salt, or isomer thereof



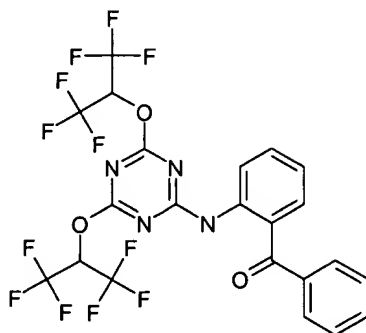
or a pharmaceutically effective derivative, salt, or isomer thereof;



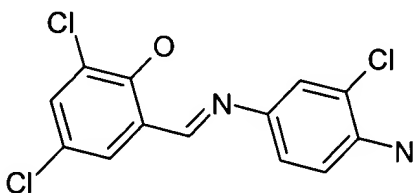
or a pharmaceutically effective derivative, salt, or isomer thereof;



or a pharmaceutically effective derivative, salt, or isomer thereof;



or a pharmaceutically effective derivative, salt, or isomer thereof; or



or a pharmaceutically effective derivative salt, or isomer thereof, in an amount sufficient to decrease said aggregates or inclusions, and wherein if said compound is haloperidol, phenazopyridine, or R-(-)-deprenyl, then said amyloidogenic protein is not beta-amyloid.

6. The method claim 1, 2, 4, or 5, wherein said cell is mammalian.

7. The method of claim 6, wherein said cell is human.

8. The method of claim 6, wherein said cell is a rodent cell.

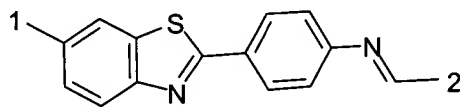
9. The method of claim 6, wherein said cell is a germ-line cell.

10. The method of claim 6, wherein said cell is *ex vivo*.

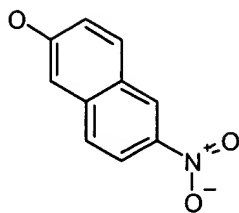
11. The method of claim 4 or 5, wherein said amyloidogenic protein is an
5 expanded polyglutamine repeat.

12. A method for treating a condition, or a symptom associated with a
condition, in a subject at risk for having an expressed expanded polyglutamine
repeat, said method comprising administering diphenyldiazo-bis-alpha-
10 naphthylaminesulfonate, or a pharmaceutically effective derivative or salt thereof,
to said subject.

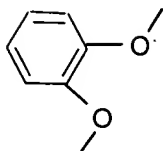
13. A method for treating a condition, or a symptom associated with a
condition, in a subject at risk for having an expressed amyloidogenic protein, said
15 method comprising administering any of bromocriptine mesylate; haloperidol;
nabumetone; primidone, hydrocortisone; phenazopyridine; R-(-)-deprenyl
hydrochloride; 6a-methylprednisolone 21-hemisuccinate; digoxin; azathioprine;
D-cycloserine; red clover; magnesium oxide; N-vanillylnonanamide; neostigmine
methyl ether; a derivative, salt, or isomer thereof; or a compound having the
20 formula selected from the any of:



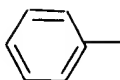
wherein 1 is CH₃ or H, and 2 is



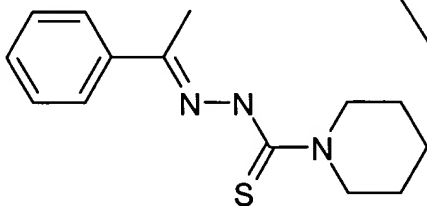
5 or wherein 1 is CH₃, and 2 is



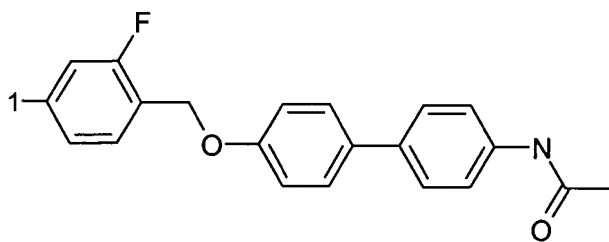
or wherein 1 is CH₃, and 2 is



or a pharmaceutically effective derivative, salt, or isomer thereof;

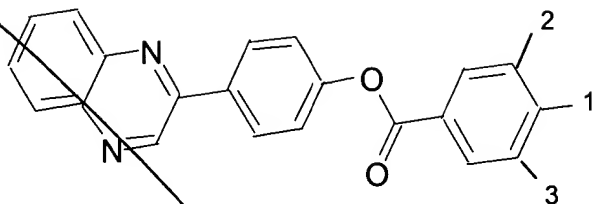


15 or a pharmaceutically effective derivative, salt, or isomer thereof;



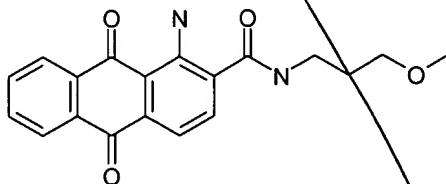
wherein 1 is H or NO₂, or a pharmaceutically effective derivative, salt, or isomer thereof;

5



wherein 1 is Cl, and 2 and 3 are H; or wherein 1 and 3 are H, and 2 is NO₂; or wherein 1 is Br, 2 is H, and 3 is NO₂; or wherein 1 is Cl, 2 is H, and 3 is Br, or a pharmaceutically effective derivative, salt, or isomer thereof;

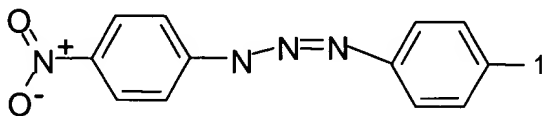
10



15

or a pharmaceutically effective derivative, salt, or isomer thereof;

20



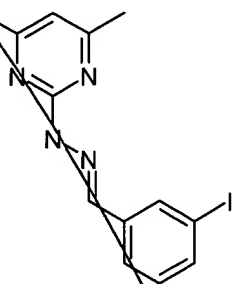
25

wherein 1 is NO₂, Br, or O₂, or a pharmaceutically effective derivative, salt, or isomer thereof;

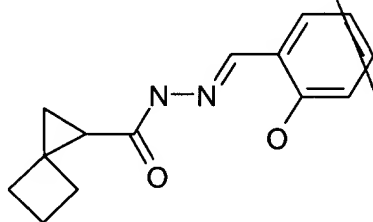
SECRET

CC(=O)Nc1ccc(cc1)-c2ccc(cc2)N=C(C)O

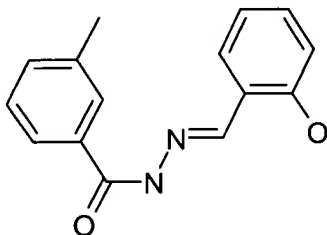
10



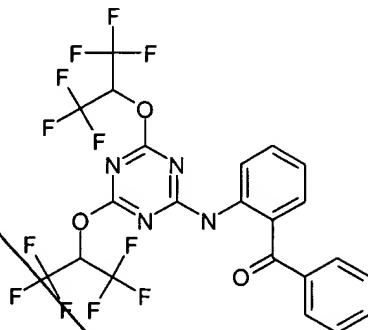
or a pharmaceutically effective derivative, salt, or isomer thereof;



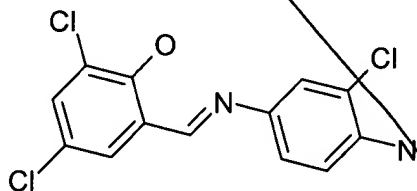
or a pharmaceutically effective derivative, salt, or isomer thereof;



or a pharmaceutically effective derivative, salt, or isomer thereof;



or a pharmaceutically effective derivative, salt, or isomer thereof; or



or a pharmaceutically effective derivative, salt, or isomer thereof to said subject.

14. The method of claim 12 or 13, wherein said condition is a neurodegenerative disease.

15. The method of claim 14, wherein said neurodegenerative disease is any of Huntington's disease, spinobulbar muscular atrophy (SBMA), spino-cerebellar ataxia type 1, spino-cerebellar ataxia type 2, spino-cerebellar ataxia type 3, spino-cerebellar ataxia type 6, spino-cerebellar ataxia type 7, dentatorubral-pallidoluysian atrophy, or familial schizophrenia.

16. The method of claim 12 or 13, wherein said condition is male infertility.

17. The method of claim 13, wherein said condition is caused by an amyloidogenic protein.

Sub 12
18. The method of claim ~~12 or 17~~, wherein said condition is caused by expanded polyglutamine repeats.

Sub 1
19. The method of claim ~~12 or 13~~, wherein said subject is a mammal.

20. The method of claim ~~18~~, wherein said subject is a human.

21. The method of claim 12, wherein said expressed expanded polyglutamine repeat is resistant to at least one of the compounds chosen from the group consisting of minocycline, daunomycin, rolitetracycline, Chrysamine G, iota-carrageenan, or dextran.

22. The method of any of claims 1, 2, or 12, wherein said derivative is any one of Direct Orange 8, Direct Yellow 26, Direct Yellow 28, Direct Blue 158, Direct Orange 6, Direct Red 1, Direct Orange 1, or Direct Black 51.

23. The method of any of claims 1, 2, 4, or 5, wherein said animals is an animal diagnosed with, or having an increased likelihood of developing a neurodegenerative disease.

24. The method of claim 23, wherein said neurodegenerative disease is any of Huntington's disease, spinobulbar muscular atrophy (SBMA), spino-cerebellar ataxia type 1, spino-cerebellar ataxia type 2, spino-cerebellar ataxia type 3,

